damaged, while the deeper portion of the hemangioma receives relatively little irradiation and, therefore, continues to grow.

C. *Gamma Rays of Radium.*—These penetrating rays which are provided by properly filtered radium pack, are most useful, and frequently even deep hemangiomata disappear with such treatment. Although the dose to the skin must necessarily be somewhat higher than the dose to the tumor with radium pack therapy, the depth dose is still satisfactory. Many hemangiomata are so sensitive that one or two doses of 700 to 1,000 gamma roentgens[6] will precipitate disappearance of the vascular tumor without damaging the skin. To obtain gamma rays we favor the use of filtered radium packs at distances of three millimeters for superficial lesions and one to three centimeters for deeper lesions. The radium must be arranged in a geometrical design, so that all portions of the tumor are irradiated as evenly as possible. To the filter of 0.5 mm. of platinum (which stops all of the beta radiation), are added 1 mm. of silver and 0.5 mm. of brass as secondary filters. The total filtration effect, therefore, is that of 1 mm. of platinum with 0.5 mm. of brass as a secondary beta ray filter.

We have not seen any undesirable results from properly filtered radium packs. Often the skin returns entirely to normal, but when it does not, the pliable pinkish-white scar which usually occurs instead is not unsightly.

D. *Radon Seeds.*—Gold-filtered radon seeds with a wall thickness of 0.2 mm. of gold and a strength of ¼ to ½ mc., can be planted in an appropriate geometrical arrangement so that there is one in every cubic centimeter of hemangioma tissue.[6] The radiation distribution is such that the skin gets less dosage than the lesion, if the seeds are planted sufficiently deep.

Frequently a single implantation of radon seeds will be sufficient to cause the hemangioma to disappear—a matter of considerable importance to patients who have come from a distance and who cannot return for numerous treatments. These tiny gold radon seeds are not removed from the tissues, but we have seen no unsatisfactory results on this account except when too many seeds were planted, or the implantations were too close to the surface.

Since radon seed implantation is a relatively simple process which frequently requires only one patient visit, it seems to us the method of choice in the therapy of the deeper hemangiomata, although we generally use heavy filtered radium packs in a preliminary attempt to determine whether the lesion is unusually radiosensitive in nature and may respond to this somewhat simpler type of treatment.

CONCLUSIONS

1. Prompt treatment of hemangiomata is indicated, because most types are more sensitive to treatment when the patients are very young. Although spontaneous regression occurs rarely, much valuable time is often lost in vainly waiting for it while the hemangiomata increase their invasive growth.

2. Unsatisfactory results in the treatment of hemangiomata are most frequently caused by the selection of the wrong agent for the particular type of hemangioma involved.

3. The "strawberry mark," and the even deeper type of cavernous hemangiomata, respond well to irradiation. Although x-ray is often satisfactory, the gamma rays of radium in the form of well filtered radium packs have given, in our experience, more uniform results. The implantation of weakly gold-filtered radon seeds permits a very favorable distribution of the radiant energy. For this reason, and because frequent repetition is not required as with other methods, radon seed implantation is often the therapy of choice.

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SODIUM SULFADIAZINE IN THE TREATMENT OF MENINGOCOCCAL MENINGITIS*

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NO deaths resulted in ten cases of epidemic meningitis treated with sulfadiazine exclusively, although six of these patients were in coma for an average of twenty-seven hours. There were slight transitory drug reactions in seven cases and temporary complications resulting from the disease in only three cases, but all patients returned to full duty in one month.

It was not until the advent of chemotherapy in the treatment of cerebrospinal meningitis and the preliminary report of the use of sulfonamides in humans by Schwentker, Gelman, and Long[1] in 1937 that the mortality rate was reduced to 10 to 12 per cent. Since that time the mortality rate has steadily decreased with this type of therapy.

CLINICAL PATHOLOGY

Although we have no autopsy material among our cases, we are aware that the pathological process appears to be readily explained by a septicemia followed by diffuse fibropurulent exudate in the meshes of the pia over the convexity and base of the brain and about the cerebellum and spinal

* The opinions and assertions contained herein are the private ones of the writers and are not to be used as official or reflecting the view of the Army Department or the army service at large.

TABLE 1.—*Symptoms Report on Ten Cases of Cerebrospinal Meningitis**

Case Numbers	1	2	3	4	5	6	7	8	9	10
Age	26	24	19	25	20	20	19	19	22	22
Nasopharyngitis	—	+	+	—	—	+	+	—	—	+
Headache	+	++	++	+	++	+	+	+	+	+
Chills	+	+	+	+	+	+	+	+	+	+
Nausea and vomiting	+	+	+	+	+	+	+	+	+	+
Photophobia	+	+	+	—	+	—	—	+	—	+
Stiff Neck (subjectively)	—	+	—	+	—	+	++	—	—	—
Length of illness before hospitalization	36 hrs.	48 hrs.	24 hrs.	12 hrs.	24 hrs.	24 hrs.	48 hrs.	18 hrs.	24 hrs.	36 hrs.

* Symptoms of patients, in coma on admission, were obtained from Field Officers.

TABLE 2.—*Clinical Findings*

Case Numbers	1	2	3	4	5	6	7	8	9	10
Coma (length of time)	7 hrs.	—	24 hrs.	5 hrs.	—	—	—	*72 hrs.	*36 hrs.	*20 hrs.
Nystagmus, V Nerve	(Strabismus)	+	+	+	+	+	+	+	+	+
Conjunctivitis	—	+	++	—	—	+	+	—	+	—
Herpes labialis	—	—	+	—	—	—	++	—	—	+
Opisthotonos	—	—	—	—	—	+	+	—	—	—
Brudzinski	++	++	+	+	+	++	+++	+	+	+
Kernig	+	+	—	—	+	+	++	*?	*?	—
Hyperactive Tendon reflex	+	+	+	+	+	+	+	+	+	++
Babinski	—	—	—	—	—	—	—	—	—	—
Petechial rash, changing to purpura	—	+	+	—	—	+	—	+	++	—
Mild clonic twitching and hyperactivity	—	—	++	—	—	—	—	++	+	+
Temperature on admission	102°	102°	103°	104°	102°	99.6°	102°	104°	104°	101°
Tachycardia, followed by bradycardia	+	+	+	+	+	+	+	+	+	+

* In coma on admission.

TABLE 3.—*Laboratory Data*

Case Numbers	1	2	3	4	5	6	7	8	9	10
Blood count WBC	13,600 90-10%	30,000 84-14%	16,000 90-10%	29,800 87-13%	21,900 86-14%	30,100 89-14%	18,350 80-20%	23,500 84-15%	43,000 90-10%	29,800 90-10%
Urine	—	—	—	—	—	—	—	—	—	—
Kahn	—	+	—	—	—	—	—	—	—	—
Blood culture	—	—	—	—	—	—	—	—	—	—
Blood sugar	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
Nasopharyngeal culture	+	+	+	+	—	+	—	*	*	+
Spinal Fluid: Pressure	280	170	310	350	325	290	350	300	400	420
Queckenstedt—normal										
Appearance	Turbid	Turbid	Turbid	Turbid	Turbid	Turbid	Turbid	Turbid	Turbid	Turbid
Count	560+ Pellicle 98% poly	1,800 100% poly	2,179 94% poly	6,250 97% poly	11,000 96% poly	1,980 91% poly	10,000 95% poly	2,850 94% poly	13,350 96% poly	10,000 90% poly
Sugar	65 mg.	83.3 mg.	71.4 mg.	35.9 mg.	62.5 mg.	5.8 mg.	6.0 mg.	62.5 mg.	40.2 mg.	26.0 mg.
Globulin	Neg.	Neg.	Inc.	Inc.	Inc.	Inc.	Inc.	Inc.	Inc.	Inc.
Smear	In. & Ex. Cellular	Ex. Cellular	In. & Ex. Cellular	In. & Ex. Cellular	Neg.†	Ex. Cellular	In. & Ex. Cellular	In. & Ex. Cellular	In. & Ex. Cellular	In. & Ex. Cellular
Culture	Neg. fluid	Pos.	Pos.	Pos.	Neg.	Neg.	Pos.	Pos.	Neg.	Neg.

* Unable to take smear.

† This case is carried as cerebrospinal meningitis because chemotherapy was started thirty-six hours before we saw him, and therefore we were unable to isolate organism.

TABLE 4.—*Subsequent Urinary Laboratory Data*

Case Numbers	1	2	3	4	5	6	7	8	9	10
Acetyl Sulfadiazine crystals	0	+	+	+	0	+	0	+	0	0
R. B. C.	Many	0	Many	Many	Many	Many	0	Many	Many	0
Albumen	++	0	+	+	++	++	0	+	+	++
Final urinalysis	—	—	—	—	—	—	—	—	—	—

cord, thus accounting for the neurological findings. Temporary conjunctivitis (Table 2) occurred in five of our cases, probably due to trigeminal[2] nerve irritation or local presence of Gram-negative diplococci, which we feel may also account for marked photophobia seen in six cases. Nystagmus from irritation or brief paralysis of the oculomotor nerves was found in all cases. Temporary deafness in the left ear of one patient occurred following involvement of the eighth nerve. Purulent arthritis[3] and synovitis were important phenomena[4] in two patients, one involving only the elbow, while the other had multiple joints affected, including both knees and right elbow, due to the septicemia.[5] Fever, chills, leukocytosis, and variable petechial rash (see pictures) which later changed to purpura,[6] were noted in five cases and were also undoubtedly due to the septicemia. The onset of the illness was initiated by nausea and vomiting in all our cases, which we feel is a paramount symptom, and has never been fully explained, but is probably due to central irritation.

TREATMENT

Although no antimeningococcic serum or meningococcic antitoxin was used, our findings concur with present statistics, that chemotherapy is far superior in the treatment of cerebrospinal menin-

gitis to serum or antitoxin, and that sulfadiazine is the drug of choice. Serum therapy should be reserved for those patients who do not respond or are sensitive to the sulfonamides. Our patients did not fall into either category.

The fulminating nature of the disease requires emergency intravenous drug therapy immediately.

In the treatment we found the initial administration[7] of 5 grams of the sodium salt of sulfadiazine, in 1,000 c.c. of triple distilled sterile water, the best method of obtaining a high blood concentration early. This method of chemotherapy was forcibly impressed upon us by the first of six cases in coma which responded dramatically. We feel that not only the bacteriostatic action was accomplished, but also replacement of fluid lost in vomiting was obtained, and chances of renal complications obviated. In order to maintain an adequate blood level of the sulfonamide, we gave the second dose of one gram in two hours by mouth when possible, thus allowing for absorption time from the intestinal tract; otherwise in four hours intravenously. All subsequent doses of one gram were given every four hours. Although the temperature dropped by crisis in two or three days, this dosage was maintained in all cases for ten days. If the patient was symptom-free, the dosage was then divided into one-half gram every four hours for three days longer, and if at this time the patient was clinically well, the chemotherapy was withdrawn entirely,[8] except where complications intervened. This may be more concisely stated;[7] continuous drug therapy until temperature normal seven days. The average total dosage of sulfadiazine was 64 grams, and the blood level was between 5 and 12 milligrams per 100 c.c. of blood for the first two weeks. We feel that the slight toxic reactions of sulfadiazine and the negligible mortality rate makes sulfadiazine the choice of sulfonamides.

At least 3,000 c.c. of fluid was given daily either by mouth or, if parenterally, 3,000 c.c. of 5 per cent glucose in normal saline. Urinalyses were determined daily, but when albumen, red blood cells, or crystals of the acetyl compound were noted (Table 4), urine examination was then done on each consecutive specimen. Then fluids were further forced to 4,000 c.c. daily and one gram of sodium bicarbonate was given four times daily to maintain an alkaline urine, thus preventing the precipitation of acetyl-sulfadiazine.[9] No permanent kidney impairment resulted under this form of therapy and adequate blood levels were maintained for as long as three weeks in one case. Daily[10] complete blood counts were taken and no depression of consequence of the hematopoietic system occurred.

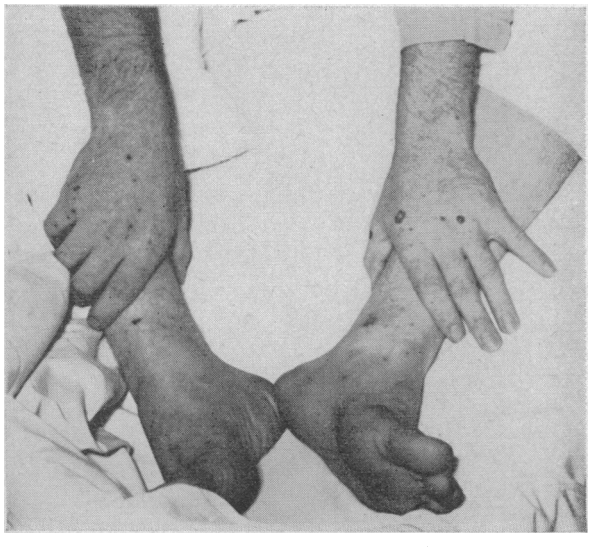

Fig. 1.—(Case 9) Petechiae after first twenty-four hours.

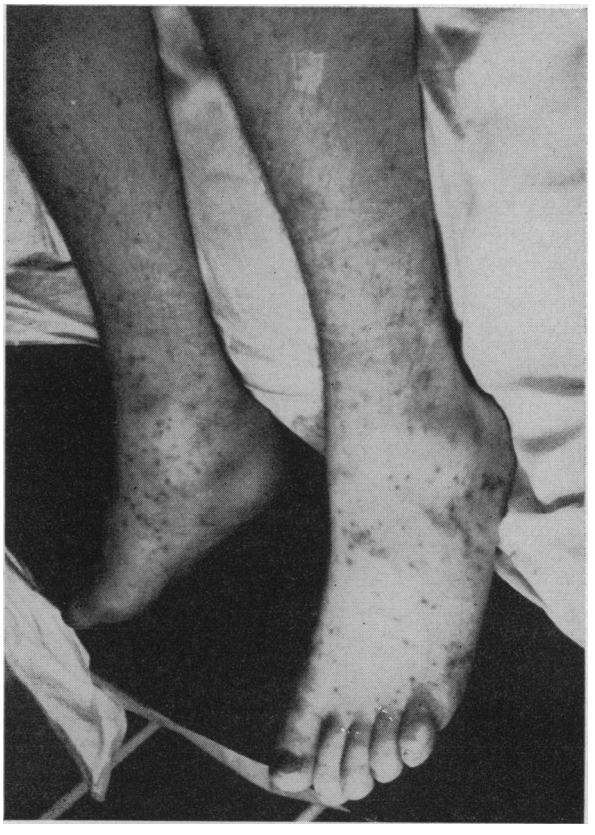

Fig. 2.—(Case 9) Petechial change after first twenty-four hours.

Blood sulfadiazine concentrations were made after the first twenty-four hours and continued on alternate days. Blood sedimentation rates were determined during convalescence, as we find from our 150 cases of chemotherapy-treated pneumonias it is an excellent criterion for complete cure before discharging soldiers to full field duty.

Chemotherapy in the treatment of cerebrospinal meningitis represents only one phase of the management of this condition. Early recognition of the symptoms (see Table 1) and prompt spinal fluid diagnosis (Table 3) are imperative. Isolation technique in a darkened quiet room offers the patient most comfort. Sedation proved to be one of the greatest problems; three of the six comatose patients had mild clonic twitchings or convulsive seizures for as long as seventy-two hours. Full restraints, even straitjackets were necessary, thus requiring alert nursing care and attention to bed

and restraint sores. It was found that the patients had a high tolerance to barbiturates, either intravenously or intramuscularly. The barbiturates were used with caution, because bradycardia followed the initial tachycardia (see Table 2). For nourishment 5 per cent glucose in saline was given to the patients in coma, and a soft diet was begun as soon as the patient was able to be fed.

Criteria for further spinal punctures were persistent clinical symptoms, or evidence of marked intracranial pressure; but in our cases there was no evidence of spinal subarachnoid block. Subsequent spinal taps at the time of discharge we found to be of no clinical value because of negative spinal fluid findings.

The routine requirement of three negative nasopharyngeal cultures, five days apart, before discharge, was followed. All patients were seen on admission and discharge by a member of the neuropsychiatric and the eye, ear, nose and throat departments.

COMPLICATIONS

The average length of hospitalization was one month, except in three cases where complications occurred. One patient (Case 7) had temporary deafness of the left ear, lasting five days. Purulent polyarthritis and synovitis were noted in another patient (Case 6), involving the right elbow and both knees. Fifty c.c. of cloudy, straw-colored fluid containing many polymorphonuclear cells was aspirated from these joints and cultured, but no meningococci were grown or seen on smears, probably due to previous bacteriostatic action of chemotherapy. In a third patient (Case 2) monoarthritis and synovitis with effusion of the left elbow developed. There were slight joint residuals clinically. The elbows affected in both arthritic cases have 15 per cent limitation of extension at the present time, but orthopedic opinion is that full function can be expected. X-ray failed to reveal skeletal changes of any permanent significance in any of the involved joints.

SUMMARY

1. No deaths resulted in ten cases of meningococcal meningitis treated with sulfadiazine exclusively, although six of these patients were in coma for an average of twenty-seven hours.

2. Constant clinical findings were: headache, nystagmus, chills, fever, nausea, vomiting, and positive Brudzinski, substantiated by laboratory findings of high blood leukocytosis and spinal fluid with high leukocytic cell count and intracellular or extracellular Gram-negative diplococci.

3. In treatment sulfadiazine is the drug of choice, because of the slight toxicity, low mortality, prompt recovery, and minimum of complications. Although no serum or antitoxin was used, we concur with present statistics that serum or antitoxin therapy should be reserved for those remote cases of drug idiosyncrasies and those who fail to respond to chemotherapy.

4. The fulminating nature of the disease requires the immediate administration of 5 grams of sodium sulfadiazine intravenously for the initial dose in all cases to obtain early high blood concentration. This should be followed by one gram every four hours intravenously if the patient is in coma or vomiting, otherwise sulfadiazine one gram orally for at least ten days. With our patients the average total dosage of sulfadiazine was 64 grams, and the blood level was between 5 and 12 milligrams per 100 c.c. of blood for two weeks. Renal and toxic complications may be obviated by ample fluids, daily complete blood counts, urinalysis, and sodium bicarbonate.

5. Complications of the disease in our cases were few with sulfadiazine and do not appear to be of a permanent nature, purulent arthritis and synovitis being most common. Without complications the average length of hospitalization was one month, discharge being based on three negative nasopharyngeal cultures taken five days apart and normal blood sedimentation rates. The latter we found, from our 150 cases of chemotherapy-treated pneumonias, to be an excellent criterion for complete cure before discharge to full field duty.

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